OIPE JC14 JUN 2 6 2005 PATENT & TRADEMARK OFFICE

**ATTORNEY'S DOCKET NUMBER: 0492479-0018 (MGH 1661.0)**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

| | | | |
|---|---|---|---|
| Applicant: | Scadden *et al.* | Examiner: | Katcheves, K. T. |
| Serial No.: | 09/803,687 | Art Unit: | 1636 |
| Filed: | March 9, 2001 | | |
| For: | *p27 and p21 in Gene Therapies* | | |

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

**DECLARATION UNDER 37 C.F.R. § 1.132**

I, David T. Scadden, declare as follows:

1. I am an inventor of the subject matter disclosed and claimed in United States patent application, Serial Number 09/803,687, filed March 9, 2001, and entitled "p27 and p21 in Gene Therapies."

2. I am a Professor in the Department of Medicine at Harvard University. I also serve as Co-director of the Harvard Stem Cell Initiative, Director of the Center for Regenerative Medicine and Technology at the Massachusetts General Hospital (MGH), and Chief of Hematologic Malignancies at the MGH. The MGH is the assignee of the above-referenced patent application. My research has focused on stem cell biology, particularly of hematopoietic stem cells, including entry and exit from the cell cycle with implication for stem cell expansion and gene transduction. A copy of my curriculum vitae is attached hereto as **Appendix A**.

3. I have read the Office Action mailed December 23, 2004, and understand that the Examiner requests further evidence regarding the invention as claimed in the present application

and specifically as it pertains to the ability of one to use antisense agents and RNAi agents in expanding a population of stem or progenitor cells based on the disclosure of the application.

4. My research group has previously shown that $p21^{Waf1/Cip1/Sdi1}$ (p21) mediates stem cell quiescence *in vivo* and decreasing p21 expression leads to an expansion of the stem cell pool. We have now demonstrated that p21 specific siRNA agents increase the gene transduction efficiency in hematopoietic stem cells while preserving cell multipotentiality.

5. Two types of RNAi were generated to silence p21 expression in target cells—*in vitro* synthesized duplex siRNA and *in vivo* expressed plasmid-derived short hairpin RNA (shRNA). See **Appendix B**. The effects of silencing p21 were studied in primary human CD34+ hematopoietic stem/progenitor cells and CMK cells derived from human megakaryoblastic cells.

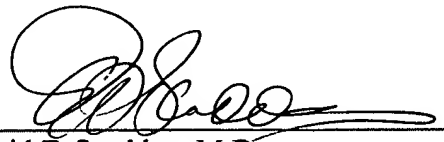
6. Both types of siRNA (Si-2 and p2.3) knocked down p21 expression by 85-98% as measured with p21 mRNA copy number using real time RT-PCR. A mismatched mutant siRNA (Si-2M) served as a specificity control and did not affect p21 expression. The RNAi effect on mRNA levels was confirmed by reduced p21 protein levels as demonstrated by Western blot. See **Appendix C**.

7. For synthesized siRNA, the level of p21 mRNA returned to baseline at 10-15 days post siRNA treatment, and for transcribed shRNA derived from the plasmid, the level of p21 mRNA was back to the pre-silencing level at 22-28 days post treatment. See **Appendix D**. Silencing p21 in a transient manner by siRNA is appealing because it limits the potential for permanent p21 deficiency contributing to malignant transformation.

8. Silencing p21 increased the efficiency of gene transduction in CD34+ hematopoietic stem/progenitor cells and preserved the multipotentiality of these cells while allowing for stable integration of gene transfer-vector into the cellular genome. Silencing p21 using RNAi may ultimately contribute to the clinical application of gene therapy in hematopoietic stem cells.

9. The data presented in the Declaration was accepted on March 17, 2005 for publication in *Gene Therapy*. The manuscript is currently in press.

10. I, David T. Scadden, declare that all statements made herein of my own knowledge are true and that these statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful, false statements and the like are made punishable by fine or imprisonment, or both, under § 1001 of Title 18 of the United States Code and that such willful, false statements may jeopardize the validity of the application or any patents that may issue thereon.



David T. Scadden, M.D.

6/17/05

Date

3923128v1

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JUN 24 2005
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# APPENDIX A

# CURRICULUM VITAE

## PART I: General Information

**DATE PREPARED**: Last updated 5/25/05 by CP


**Name:** David T. Scadden, M.D.

**Office Address:** 185 Cambridge Street, CPZN 4265A, Boston, MA. 02114

**Office Telephone:** (617) 726-5615

**Home Address:** 62 Lexington Street, Weston, MA. 02193

**E-Mail:** scadden.david@mgh.harvard.edu **FAX:** (617) 726-2662


**Place of Birth:** Passaic, New Jersey

**Education:**

| | | |
|---|---|---|
| 1975 | B.A. | Bucknell University (English) |
| 1975-1976 | | Columbia University (Pre-Medical Studies) |
| 1980 | M.D. | Case Western Reserve School of Medicine |
| 2004 | A.M. | Harvard Medical School (Honorary) |

**Postdoctoral Training:**

Internship and Residencies:

| | | |
|---|---|---|
| 1980-1981 | Intern | Brigham and Women's Hospital, Boston, MA. |
| 1981-1982 | 2nd year Medical Resident | Brigham and Women's Hospital, Boston, MA. |
| 1982-1983 | 3rd year Medical Resident | Brigham and Women's Hospital, Boston, MA. |

Clinical and Research Fellowships:

| | | |
|---|---|---|
| 1980-1984 | Clinical Fellow in Medicine | Harvard Medical School |
| 1983-1984 | Clinical Fellow in Hematology/Oncology | Brigham and Women's Hospital, Dana-Farber Cancer Institute |
| 1984-1986 | Research Fellow in Medicine | Harvard Medical School |
| 1985-1987 | Research/Clinical Fellow in Medicine | Brigham and Women's Hospital (JM Cunningham, mentor) |
| 1987-1988 | Research Fellow | New England Medical Center (RS Schwartz & JM Coffin, mentors) |

**Licensure and Certification:**

| | |
|---|---|
| 1980 | Diplomate, National Board of Medical Examiners |
| 1983 | Massachusetts License Registration |
| 1983 | Diplomate, American Board of Internal Medicine |
| 1985 | Diplomate, Subspecialty Board in Medical Oncology |
| 1988 | Diplomate, Subspecialty Board in Hematology |

**Academic Appointments:**

| | | |
|---|---|---|
| 1986-1987 | Instructor in Medicine | Harvard Medical School |
| 1987-1988 | Instructor in Medicine | Tufts University School of Medicine |
| 1988-1991 | Instructor in Medicine | Harvard Medical School |
| 1991-1995 | Assistant Professor of Medicine | Harvard Medical School |
| 1995-2003 | Associate Professor of Medicine | Harvard Medical School |
| 2003- | Professor of Medicine | Harvard Medical School, Harvard University |

**Hospital or Affiliated Institution Appointments:**

| | | |
|---|---|---|
| 1988-1996 | Active Staff | Deaconess Hospital, Boston, MA. |
| 1988-1993 | Courtesy Staff | St. Luke's Hospital of New Bedford, MA. |
| 1995-1996 | Courtesy Staff | Waltham-Weston Hospital, Waltham, MA. |
| 1995-2001 | Associate Physician | Massachusetts General Hospital, Boston, MA. |
| 1997-2005 | Staff Physician, Hematology/Oncology | Brigham and Women's Hospital, Boston, MA. |
| 1997- | Staff Physician, Hematology/Oncology | Dana-Farber Cancer Institute, Boston, MA. |
| 2001- | Physician | Massachusetts General Hospital, Boston, MA. |

**Other Professional Positions and Major Visiting Appointments:**

| | | |
|---|---|---|
| 1985-1987 | Associate | Howard Hughes Medical Institute, Boston, MA |

**Major Administrative Responsibilities:**

| | |
|---|---|
| 1993-1995 | Director, AIDS Hematology/Oncology Research Unit, Deaconess Hospital |
| 1995- | Director, Experimental Hematology, Massachusetts General Hospital |
| 1995-2004 | Co-Director, AIDS Research Center, Massachusetts General Hospital |
| 1995-1997 | Mentoring Committee, Dana-Farber/Partners Cancer Care |
| 1996- | Chair, Immunodeficiency Disease Center, Dana-Farber/Partners Cancer Care |
| 1996-2000 | Steering Committee, Hematologic Malignancies, Dana-Farber/Partners Cancer Care |
| 1996-2001 | Scientific Review Committee, Dana-Farber/Partners Cancer Care |
| 1996-1999 | Mallinckrodt General Clinical Research Center (GCRC) Advisory Committee Member, Massachusetts General Hospital |
| 1997-1998 | Fellowship Selection Committee, Hematology/Oncology, Dana-Farber/Partners Cancer Care |
| 1998- | Committee of Immunology, Harvard Medical School, Program in Immunology |
| 1999- | External Advisory Committee, The Connell O'Reilly Cell Manipulation and Gene Transfer Laboratory, Dana-Farber Harvard Comprehensive Cancer Center |
| 2000- | Chair, Oncology Clinical Recruitment Committee, Massachusetts General Hospital |

| | |
|---|---|
| 2000- | Director, Hematologic Malignancies Program, Massachusetts General Hospital |
| 2000- | Co-director, Partners/Fenway/Shattuck Center for AIDS Research |
| 2000-2001 | Intern Selection Committee, Massachusetts General Hospital |
| 2000-2004 | Executive Committee Member, Harvard Medical School Division of AIDS (HMSAIDS) |
| 2001- | Cancer Center Advisory Board, Massachusetts General Hospital Cancer Center |
| 2002- | Member, National Cancer Institute Board of Scientific Counselors, National Institutes of Health |
| 2002- | Director, Center for Regenerative Medicine and Technology, Massachusetts General Hospital |
| 2004- | Co-Director, Harvard Stem Cell Institute, Harvard University |
| 2005- | Member, Biological and Biomedical Sciences Program, Harvard Medical School |

**Major Committee Assignments:**

| | |
|---|---|
| 1990 | Ad hoc review committee, "Clinical Research in AIDS", National Institutes of Health |
| 1993-1995 | Oncology Core Committee, ACTG, NAIAD |
| 1994 | Ad hoc review committee, "Basic Research on Hematopoietic Stem Cell Biology", National Institute on Diabetes and Digestive and Kidney Diseases |
| 1994 | Ad hoc review committee, "Studies of the viral etiology of AIDS-associated malignancies", National Cancer Institute |
| 1994-1995 | Research Agenda Committee, ACTG, NIAID, "Complications of HIV." |
| 1995 | Ad hoc review committee, "Cytokines Effects on Hematopoiesis in AIDS Animal Models", National Heart, Lung, and Blood Institute |
| 1995-present | AIDS Malignancy Consortium, Steering Committee, National Cancer Institute |
| 1995-1999 | AIDS Malignancy Consortium, Lymphoma Working Group, Chair, National Cancer Institute |
| 1996 | Ad hoc reviewer, National Heart, Lung, and Blood Institute, Hematology 2 Study Section |
| 1996-2000 | AIDS Malignancy Working Group, Chair, Clinical Investigation, National Cancer Institute |
| 1997 | Ad hoc reviewer, Hematology-2 Study Section, National Institutes of Health |
| 1998 | Task Force on Integration of Adult HIV/AIDS Clinical Trials Networks, Office of AIDS Research, National Institutes of Health |
| 1998 | DaunoXome and AmBisome Advisory Board, NeXstar Pharmaceutical |
| 1998 | External Advisory Board, University of Colorado BMT Program Project |
| 1998 | Advisory Board, HMS SCOR in Hematologic Disease |
| 1998- | Scientific Review Committee, Member, Concert for the Cure, Boston, MA |
| 1998 | Outside Reviewer, Dutch Cancer Society |
| 1999 | Program Project Review Committee, Member, National Institutes of Health |
| 1999 | Ad hoc Scientific Review Committee, Member, National Institutes of Health, "Clinical Research Studies." |
| 2000- | AIDS Malignancy Consortium, Executive Committee, Chair, National Cancer Institute |
| 2000 | Site Visit Team, Member, HIV/AIDS Malignancy Branch, National Institutes of Health |
| 2000 | Finance Task Force, Committee Member, American Society of Hematology |

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|---|---|
| 2000 | Site Visit Team Member, NCI Medicine Branch, Department of Experimental Transplantation and Immunology, National Institutes of Health |
| 2000 | Steering Committee Member, AFM/Harvathon Gene Therapy Initiative |
| 2001 | Etiology and Pathogenesis Planning Workshop Member, FY 2003 NIH Plan for HIV-Related Research, Office of AIDS Research, National Institutes of Health |
| 2001 | Outside Reviewer, Hematology-2 Study Section, National Institutes of Health |
| 2001 | Outside Reviewer, AIDS and Related Research-6, National Institutes of Health |
| 2001 | Outside Reviewer, Wellcome Trust |
| 2001- | Standing Review Panel, Member, Doris Duke Charitable Foundation's Clinical Scientist Development Award Program |
| 2001-2004 | Committee on Investment & Audit, Member, American Society of Hematology |
| 2001 | Outside Reviewer, AIDS Research Review Committee, National Institute of Allergy and Infectious Disease, National Institutes of Health |
| 2001- | Ad hoc Clinical Search Committee, Brigham and Women's Infectious Disease Division, Partners AIDS Research Program |
| 2001 | Honorary Consultant, Chinese Foundation for Prevention of STD and AIDS |
| 2002- | AIDS Malignancy Lab Working Group, Co-Chair, Clinical Investigation, National Cancer Institute |
| 2002 | Honorary Consultant, Institute of Hematology, Tianjin, China |
| 2002 | Grant Review Committee Chair, National Cancer Institute of Canada |
| 2002- | Scientific Advisory Board member, Harvard Gene Therapy Initiative |
| 2003 | Scientific Advisory Board member, Center for Cutaneous Biology, Massachusetts General Hospital |
| 2003- | Ad hoc recruitment committee, Hematology Division, Brigham & Women's Hospital |
| 2003- | Ad hoc recruitment committee for Assistant Director, Blood Transfusion Service, Massachusetts General Hospital |
| 2003- | Ad hoc recruitment committee for Director, Wellman Labs, Massachusetts General Hospital |
| 2003- | Ad hoc recruitment committee for Director, Hematologic Malignances, Massachusetts General Hospital and Professor, Harvard Medical School |
| 2003 | Site Visit Team, Member, Viral Epidemiology Branch, National Institutes of Health |
| 2003- | Immunology Scientific Advisory Board member, New England Primate Research Center, Harvard Medical School |
| 2004- | Data Safety Management Board, Alexion Pharmaceuticals |
| 2004 | Panel Member, Tumor Stem Cells and the Genetic Basis of Self Renewal Think Tank, National Cancer Institute, National Institutes of Health |
| 2004 | Site Visit Team, Chair, HIV/AIDS Malignancy Branch, National Institutes of Health |
| 2004-2005 | Member, Committee on Establishing a National Cord Blood Stem Cell Bank Program, Institute of Medicine, The National Academies |
| 2004- | Ad hoc faculty search committee for Center for Human Genetic Research, Massachusetts General Hospital and Associate Professor, Harvard Medical School |
| 2004- | Ad hoc faculty search committee for New England Primate Research Center, Harvard Medical School and Assistant Professor, Harvard Medical School |
| 2004- | Ad hoc faculty search committee for Cardiovascular Division, Brigham & Womens Hospitaln and Professor of Medicine, Harvard Medical School |
| 2004- | Member, Advisory Board, International Society for Stem Cell Research |

2005- Member, Scientific Advisory Board, Division of John Hopkins in Singapore

**Professional Societies:**

1983- American Association for the Advancement of Science, Member
1986- American Association for Cancer Research
1988- Massachusetts Medical Society, Member
1988- American Society for Clinical Oncology, Member
1989- American College of Physicians, Member
1990- American Society of Hematology, Member
1992- American Society of Microbiology, Member
1992- International Society of Experimental Hematology, Member
1996- American Society for Clinical Investigation, Member
1997- American Society of Gene Therapy, Member
1998- Harvard Medical School, Program in Immunology, Member
2002- Association of American Physicians, Member
2003- International Society for Stem Cell Research, Member

**Community Service Related to Professional Work:**

1983– Pre-medical Advisor Committee, Senior Common Room Member, Dudley House, Harvard College
1995- Biology Mentor Program, Weston High School
2003- Scholars in Clinical Science Program, Harvard Medical School
2005- Member, Dept. of Surgery Research Council Junior Faculty Mentoring Program
2005- Mentor, Health Sciences and Technology Division, Harvard and MIT, MD/MEMP students

**Editorial Boards:**

1992- New England Journal of Medicine, Ad hoc reviewer
1992- Journal of Clinical Oncology, Ad hoc reviewer
1993- AIDS, Member
1993-1995 Cytokines in Hematology/Oncology, Member
1993- American Journal of Hematology, Ad hoc reviewer
1993- Cancer, Ad hoc reviewer
1993- Blood, Ad hoc reviewer
1993- Experimental Hematology, Ad hoc reviewer
1994- Science, Ad hoc reviewer
1994- Proceedings National Academy of Sciences, U.S.A., Ad hoc reviewer
1995- Nature Medicine, Ad hoc reviewer
1995- Journal of Virology, Ad hoc reviewer
1995- Journal of Acquired Immunodefiency Disease, Ad hoc reviewer
1997- Human Gene Therapy, Ad hoc reviewer

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| 1997 | Gene Therapy, Ad hoc reviewer |
| 1998- | Nature Biotechnology, Ad hoc reviewer |
| 1998- | Journal of Clinical Investigation, Ad hoc reviewer |
| 1998- | AIDS Research and Human Retrovirus, Ad hoc reviewer |
| 1999- | Cancer Gene Therapy, Ad hoc reviewer |
| 2002- | Molecular and Cell Biology, Ad hoc reviewer |
| 2002- | Leukemia, Ad hoc reviewer |
| 2001- | Journal of Immunology, Ad hoc reviewer |
| 2002- | Journal of Leukocyte Biology, Ad hoc reviewer |
| 2003- | Stem Cells, Editorial Board Member |
| 2003- | Experimental Hematology, Editorial Board Member |
| 2003- | Blood, Associate Editor |
| 2004- | Immunity, Ad hoc reviewer |
| 2004- | Nature Immunology, Ad hoc reviewer |
| 2004- | Genes and Development, Ad hoc reviewer |
| 2004- | Development, Ad hoc reviewer |
| 2004- | Journal of Cell Biology, Ad hoc reviewer |
| 2004- | Nature Cell Biology, Ad hoc reviewer |
| 2005- | Journal of Stem Cells, Editorial Board member |

**Awards and Honors:**

| | |
|---|---|
| 1973 | Phi Alpha Theta, International History Honor Society, Bucknell University |
| 1975 | B.A. Cum Laude with Honors in English Literature, Bucknell University |
| 1979 | Alpha Omega Alpha, National Honor Medical Society, Case Western Reserve School of Medicine |
| 1980 | Edwin C. Garvin, M.D., Senior Prize, Case Western Reserve School of Medicine |
| 1988 | Physician Scientist Award, National Institutes of Health |
| 1995 | Saltonstall Scholar of Medicine, Massachusetts General Hospital, Harvard Medical School |
| 1996 | American Society of Clinical Investigation, elected |
| 2001 | Doris Duke Innovation in Clinical Research Award |
| 2001 | Honorary Consultant, Chinese Foundation for the Prevention of STD and AIDS |
| 2002 | Burroughs Wellcome Fund Clinical Scientist in Translational Research Award |
| 2002 | Association of American Physicians, elected |
| 2002 | Honorary Professor, Institute of Hematology, Peking Union Medical College, Chinese Academy of Medical Sciences |
| 2002 | Interurban Clinical Club, elected |
| 2002 | Alan Goldfine Leadership Chair of Research, Brain Tumor Society |
| 2004 | Leukemia and Lymphoma Society, Translational Research Award |

## PART II. Research, Teaching and Clinical Contributions

### A. Narrative Report:

I started my research career focusing on retroviruses as a pathogenic model for hematologic disease as a post-doctoral fellow in the Howard Hughes laboratory of Dr. James M. Cunningham. The AIDS

epidemic was then at full force and my research evolved into a focus on HIV. During the 1990s, I developed a program of patient care, clinical trials and basic investigation while at the then Deaconess Hospital and eventually at the MGH. The clinical research program has contributed a standard of care for advanced Kaposi's sarcoma (paclitaxel)(*J Clin Oncol*), played a role in studies that resulted in three new FDA approved therapies and engaged patients in trials that defined underlying immunologic and hematologic function in AIDS (*J Immunol, Blood*). My role in the field included national and international administrative activities such as Chairmanship of the NCI-sponsored AIDS Malignancy Consortium and involvement on NCI advisory panels and for international organizations.

AIDS complications in the U.S. have waned and my emphasis has moved from hematopoietic cells as viral targets to potential therapeutic tools. I decided that ultimately making a difference in AIDS involves rebuilding the immune system and have focused on doing so from the stem cell up. My lab has worked on the physiology of primitive cells in HIV infection and provided definitive molecular evidence that hematopoietic stem cells are sanctuary cells, uninfectible by the virus (*Blood, J Virol*). This led to detailed molecular characterization of the stem cell (*Science*) and definition of gene expression changes as normal, primary human stem cells underwent lineage specific differentiation (*Proc Natl Acad Sci USA*). These studies were the platform for subsequent work on stem cell regulation.

We sought to address the question of what dictates the characteristic quiescence of stem cells? Using comparative gene expression analysis in functionally defined subsets of cells, we identified candidates and then subsequently defined that the cyclin dependent kinase inhibitor, $p21^{cip1/waf1}$, serves as a critical molecular switch (*Science*). Absent this gene product, stem cells more rapidly cycle and are more abundant in vivo. In addition, without this molecule, stem cells deplete prematurely under conditions of stress leading to animal mortality. We therefore defined a molecular contributor to stem cell quiescence and provide evidence that quiescence is a physiologic imperative for longevity.

We then asked whether other cyclin dependent kinase inhibitors participate in stem cell regulation. We demonstrated that despite molecular similarities, $p27^{kip1}$ plays an entirely distinct role in hematopoiesis. We showed that $p27^{kip1}$ functions at the more mature progenitor level markedly affecting the size of that cell pool (*Nature Medicine*). These differentiation stage specific effects of $p21^{cip1/waf1}$ and $p27^{kip1}$ had not been previously recognized.

To address whether these mediators of cell cycle control were dictated by external factors, we assessed cell surface expressed candidate gene products. We defined that TGFbeta influences cell cycling independent from either p21 or p27 (*Blood*). We showed however that Notch1 receptor activation enhanced self-renewal of stem cells *in vivo* and altered the balance of lymphoid and myeloid differentiation (*Blood*). We further defined a G protein-coupled receptor of the purine/pyrimidine receptor family (P2Y), GPR105, restricted in expression to quiescent hematopoietic stem cells and functioning in cell migration (*Genes and Development*). These studies provided evidence for Notch as a key mediator of stem cell function *in vivo* and identified a new class of receptors modulating the stem cell compartment. We reported a series of studies on stem and hematopoietic cell localization including mechanisms for chemokine receptor mediated mature cell egress from organs of differentiation (*Nature Medicine, J Clin Invest, Nature Biotechnol, J Immunol, Blood)*. In addition, we developed techniques for the isolation (*Nature Biotechnol)*, targeted T cell differentiation (*Nature Medicine, Nature Biotechnol)* and in vivo tracking of stem cells (*Nature Biotechnol),* each with potential clinical implications.

Stem cell regulation is largely dictated by events in the microenvironmant, but the stem cell niche in vivo had not been defined. We reasoned that the bone marrow resided in bone due to a regulatory relationship of bone to hematopoiesis and demonstrated through an animal model that specific activation of osteoblasts increased the stem cell pool in vivo. We defined that this was mediated by Notch1 activation and could be recapitulated by osteoblast activation using parathyroid hormone. This manipulation could increase stem cell numbers in vivo, increase stem cells in ex vivo culture and provide substantial improvement in animal survival following bone marrow transplantation (*Nature*). These data provide definition of osteoblasts as part of the stem cell niche in vivo and show that manipulating the niche, rather than the stem cell directly, can influence stem cell outcomes. Further they provide a strategy for affecting stem cell based therapies, using an available drug, providing a ready avenue of translation into the clinic.

In sum, my activities in AIDS hematology/oncology generated at the height of the epidemic have now been modified to focus on hematopoietic stem cells. I am committed to creating a program where basic understanding of stem cell regulation can be put to practical use in clinical settings, particularly in the context of cancer and AIDS. In doing so, I believe we can foster the basis for bringing developmental biology to medicine, creating an environment in which laboratory and clinical investigators can train, find fertile opportunity for innovative ideas and use an existing infrastructure to put concepts into practice.

**B. Funding Information:**

| | |
|---|---|
| 02/88-02/91 | National Institutes of Health: PI<br>Physician Scientist Award, National Cancer Institute. |
| 10/90-12/93 | Sandoz: PI<br>A Phase I, Open-label Trial of SDZ ILE 964 (RhIL-3) in AIDS Patients With Cytopenia. |
| 11/90-10/94 | Amgen: PI<br>Consensus Interferon Alpha for AIDS-associated Kaposi's Sarcoma. |
| 02/91-07/96 | National Institutes of Health: RO1-HL44851/PI<br>Mechanisms of Hematopoiesis in AIDS. |
| 07/91-01/95 | National Institutes of Health: RO1-CA55520/PI<br>Biological Approaches to AIDS Lymphoma. |
| 03/92-11/95 | Genentech: Co-PI<br>Exploratory Studies on Hematopoiesis and Megakaryocytopoiesis. |
| 04/92-04/95 | Immunex: PI<br>Recombinant Human Granulocyte - Macrophage Colony Stimulating Factor ("rhuGm-CSF") to Modulate the Antiviral Efficacy of Zidovudine (AZT). |

06/92-04/95 Immunogen: National PI
Treatment of HIV-associated NHL Using Modified mBACOD Chemotherapy Plus the Immunoconjugate Anti-B4-blocked Ricin.

08/92-09/95 Vestar: PI
DaunoXome vs. Combination Chemotherapy ABV for Kaposi's Sarcoma.

04/93-06/94 Hoffman-La Roche: PI
A Phase II Study of Oral TAT Antagonist for AIDS-associated Kaposi's Sarcoma.

08/93-06/95 Amgen: PI
Randomized, Controlled, Multicenter Trial of Filgrastim for Neutropenia in Patients with AIDS.

09/93-09/96 National Institutes of Health: RO3-CA62686/PI
Immunoconjugate Therapy for Relapsed AIDS Lymphoma.

09/93-09/98 National Institutes of Health: RO3-CA62776/PI
Adoptive Immunotherapy for AIDS Lymphoma.

01/94-09/95 Immunogen: National PI
Anti-B4-blocked ricin plus CHOP chemotherapy for AIDS Lymphoma

01/94-10/95 ID Biomedical: PI
Cycling Probe Reaction Evaluation for HIV-1.

07/94-06/95 AmFar - Co PI
*In vitro* models of immune reconstitution in HIV.

08/94-04/98 National Institutes of Health, NIAID: RO1-A136550/Co-PI
MGH/awarding institution, Immune Reconstitution in AIDS virus infection.

11/94-07/98 Ilex: PI
MGBG for relapsed AIDS Lymphoma

12/94-11/95 Clark Foundation: PI
*In vitro* models of gene therapy for AIDS.

08/95-07/00 National Institutes of Health: RO1-DK50234/PI
Functional Isolation of Human Hematopoietic Stem Cells.

09/0/-08/06 National Institute Of Health: PO1-DE14388-03 (Wang)
Oral T Cell Responses to EBV, KSHV and HIV

09/95-04/00 National Institutes of Health: RO1-HL55718/PI
Comparative Biology of Hematopoietic Stem Cells.

09/95-07/04 National Institutes of Health: UO1-CA71375-09S1 (Scadden)
Boston AIDS Malignancies Consortium.

02/96-04/97 Ligand: PI
LGD 1057 for Kaposi's sarcoma, Phase I, II

04/96-04/98 Ligand: PI
AR 1057 for Kaposi's sarcoma Phase III

8/96-07/01 National Institutes of Health: RO1-HL44851/PI
Mechanisms of Hematopoiesis in AIDS.

09/96-07/02 National Institutes of Health: RO1-CA73580/PI
Immunobiology of HHV-8 in Kaposi's sarcoma.

02/97-04/98 Baker-Norton: PI
Paclitaxel for Kaposi's sarcoma

03/97-02/99 Cytran, Inc.:PI
IM-862 product nasal solution open label protocol for evaluation of treatment in Kaposi's sarcoma.

04/97-03/01 Department of Defense, DARPA: 9624-FP-111/PI
Immune Cell-based countermeasures to biologic pathogens and myelotoxins.

09/02-03/05 DAMD 17-02-C-0125337 (Craiu)
DARPA (subcontract)
Novel meyhods for stem cell isolation and stem cell fate decisions, in support of the ex Vivo immune system

05/97-04/99 Cell Genesys:PI
Pilot study of autologous CD4-zeta gene-modified T cell infusion with or without IL-2 in patients with HIV infection.

05/97-04/99 Cell Genesys: PI
Phase II study of autologous CD4-zeta gene-modified T cells with or without exogenous interleukin-2 in HIV-infected patients.

08/97-07/98 Bristol-Meyers Squibb:PI
Paclitaxel for patients with AIDS-associated Kaposi's sarcoma

08/97-07/98 Immunex, Inc.:PI
Phase III double blind placebo controlled trial of recombinant human GM-CSF in patients with advanced HIV disease

04/98-03/99 Cell Genesys: PI
Phase II study of autologous CD4-zeta gene-modified T cells in HIV infected patients with undetectable plasma viremia on combination antiretroviral drug therapy.

07/98-06/02 National Institutes of Health: K12- CA77845-01/PI
Boston AIDS Oncology Training Program.

07/98-05/01 National Institutes of Health: PO1-CA78378 (Anderson)
Novel immune-based therapies for multiple myeloma.

10/98-11/99 SyStemix, Inc.: PI
A Phase I/II study in HIV-1 infected patients infused with CD34++Thy+hematopoietic stem cells (HSC) from G-CSF mobilized peripheral blood retrovirally transduced with RevM10/antisense POLI.

10/98-11/99 SyStemix, Inc.: PI
A Phase I/II study of the Safety & Feasibility of RevM10 transduced hematopoietic stem cells in HIV-related non-Hodgkin's lymphoma patients already being treated with high dose chemotherapy.

03/99-07/03 National Institutes of Health/SBIR/Co-PI
Science Research Laboratory (MGH subcontract)
Purging progenitor cell preparations by pulsed electric fields.

09/99-07/03 National Institutes of Health: U01 CA70019-05 (Lee)
AMC Operations Center – Supplement

08/01-07/03 National Institutes of Health: U01 CA70019-07 (Lee)
Chair of AMC Lymphoma Working Group

07/00-10/01 NASA/SBIR/Science Research Laboratory (Craiu)
Microgravity Enhanced Biological Cell Selection

08/00-07/03 National Institutes of Health: U01 CA70019-07 (Lee)
T Cell Responses to KSHV in Mother to Child Transmission

08/01-07/03 National Institutes of Health: U01 CA70019-07 (Lee)
AMC supplement 14/ International Infrastructure

08/00-07/05 National Institutes of Health: P50 CA86355-04 (Weissleder)
Center for Molecular Imaging Research

09/00-08/05 National Institutes of Health: P30 AI42851 (Walker)
Partners/Fenway/Shattuck Center for AIDS Research

12/00-11/05 National Institutes of Health: P01 AI29530 (Ritz)

Modeling T-cell Neogenesis after Allogeneic Stem Cell Transplantation

02/01-01/06 National Institutes of Health: R01 HL65909-04 (Scadden)
Targeted Manipulation of Stem Cells for AIDS Therapy

04/01-03/06 National Institutes of Health: R01 DK50234-07 (Scadden)
Functional Isolation of hematopoietic stem cells

08/95-03/05 National Institutes of Health: R01 DK50234-10 (Scadden)
Functional Isolation of Human Hematopoietic Stem Cells (Supplement)

07/01-06/04 Doris Duke Charitable Foundation: Innovation in Clinical Research Award
Stem Cell Expansion Through Manipulation of p21Cip1

07/02-06/07 Burroughs Wellcome Fund: Clinical Scientist Award in Translational Research
Developing Control Mechanism-Based Stem Cell Therapies

02/91-07/06 National Institutes of Health: RO1-HL44851-14/ (Scadden)
Mechanisms of Hematopoiesis in AIDS.

01/04-12/04 The Foundation For A Cure For Mitochondrial Disease, Inc. (Scadden)
Stem Cell Transplant Therapy for Treating Mitochondrial Disease

04/03-03/08 National Institute of Health: RO1-HL070866-02 (Jones)
FIO2 and Blood Vessel Formation in Adult Lung

05/04-04/05 (Seiden) PI
DFHCC/Howard Hughes Spores Subcontract Project 4

10/04-09/07 Leukeima and Lymphoma Society 6178-05 (Scadden)
Therapeutic Manipulation of the stem cell niche

10/04-05/07 DARPA (subcontract) (Craiu)
Ex-vivo Functional Bone Marrow and thymic Microenviroment

**C. Report of Current Research Activities**

Stem cell biology is the major focus of my current research effort. Specifically, the lab continues to emphasize cell cycle control with an emerging emphasis on understanding the interaction of stem cells with their microenvironment in affecting cell phenotype. We have systematically assessed how a series of cyclin dependent kinase inhibitors can influence the kinetics and pool size of the hematopoietic stem cells and shown that by knocking down expression of at least one such molecule (p21) stem cell expansion can proceed. We are collaboratively investigating the link between Notch1 activation and CDKIs defining a molecular pathway joining them to account for the synergistic effect on stem cell pools. Our interaction with tissue engineering expertise in the nascent Center for Regenerative Medicine

and Technology is particularly timely for the increasing emphasis on how stem cells are guided by their environment. To define how stem cell location in bone marrow may be affected by bone, we have established collaborative relationships with bone biologists. Through these interactions, we have tested genetic alterations of bone constituents and their impact on stem cells. These results have defined that the cellular, mineral and matrix constituents of bone alter the localization, proliferation or survival of hematopoietic stem cells. These studies are ongoing and provide the first defined elements of a microenvironmental niche in controlling the behavior of mammalian stem cells.

The clinical research emphasis of my program has decreased with the changes in the HIV epidemic, but I continue to remain active in the development and conduct of clinical studies in AIDS related malignancies. Specifically, I am the national chair on a multi-institutional bone marrow transplant study for relapsed AIDS lymphoma and a phase III trial for up-front therapy of AIDS lymphoma. I am involved in studies on Kaposi's sarcoma here in the U.S. and in South Africa and continue to provide input to understanding immunologic aspects of KSHV infection now guided by a former trainee. As stem cell based therapies are enabled by my laboratory effort, reconstituting HIV resistant immune function in AIDS is our planned target.

**D. Report of Teaching:**

1. Local Contributions

   a. Harvard Medical School Courses

| | |
|---|---|
| 1988-1989 | Introduction to Clinical Medicine<br>Preceptor<br>Two medical students/year, 10 hours prep/15 hours contact |
| 1994 | Hematology Pathophysiology (New Pathway HMS II)<br>Tutor<br>Eight medical students/year in tutorial<br>Twenty students in section<br>Three weeks/year, 12 hours prep /18 hours contact |
| 1994 | Hematology Pathophysiology (New Pathway HMS II)<br>Section instructor<br>Fifteen students per section<br>Three weeks/year, 6 hours prep /9 hours contact |
| 1995 | Hematology Pathophysiology (New Pathway HMS II)<br>Section instructor<br>Fifteen students per section<br>Three weeks /year, 6 hours prep /9 hours contact |
| 1998 | Design and Conduct of Clinical Trials<br>Faculty member<br>25 Fellows |

Six weeks/year, 2 hours prep /2 hours contact

c. Local invited teaching presentations:

1988-present Hematology Consult and In-patient Attending
Attending
One Fellow, 0-1 Resident, 0-1 Student
One month/year, 4 hours prep /25 hours contact

1988-1992 Oncology Consult and In-patient Attending
Attending
One Fellow, 0-1 Resident, 0-1 Student
One month/year, 4 hours prep/25 hours contact

1989 Medical Services Attending
Two Students, 3 Residents
One month, 6 hours prep/20 hours contact

1989 Medical Grand Rounds Lecturer
Residents, Fellows, Staff/50 Attendees, 2 hours prep/1 hour contact

1993 Grand Rounds
Two affiliated teaching hospitals: AIDS Hematology/Oncology
Tumor Board: Oncology teaching hospital, "AIDS malignancies."
Research Rounds: Two affiliated teaching hospitals, "Molecular studies of hematopoiesis."
10-30 attendees, 4 hours prep/4 hours contact

1994 Hematology/Oncology Grand Rounds: Longwood Medical Area Hospitals, "AIDS-related malignancies."
80 attendees, 3 hours prep/1 hour contact

Invited Speaker: Newton Wellesley Hospital, "AIDS-related malignancies."
30 attendees, 1 hour prep/1 hour contact

1995 Medical Grand Rounds: Deaconess Hospital, "AIDS-related malignancies."
100 attendees, 3 hours prep/1 hour prep

Oncology Grand Rounds: New England Medical Center, "HIV-related malignancies; management and epidemiology."
50 attendees, 1 hour prep/1 hour contact

Infectious Disease Grand Rounds: Massachusetts General Hospital, "AIDS-related malignancies."
20 attendees, 2 hours prep/1 hour contact

Medical Grand Rounds: Lahey Clinic, "Functional isolation and characterization of human hematopoietic stem cells."
20 attendees, 2 hours prep/1 hour contact

Medical Grand Rounds: Waltham/Weston Hospital, "AIDS-related malignancies."
20 attendees, 1 hour prep/1 hour contact

Transfusion Rounds: Brigham and Women's Hospital, "Functional isolation and characterization of human hematopoietic stem cells."
30 attendees, 1 hour prep/1 hour contact

Medical Grand Rounds: Cambridge Hospital, "AIDS malignancies overview and update."
25 attendees, 1 hour prep/1 hour contact

Invited Speaker: St. Elizabeth's Hospital, "The functional isolation and characterization of human hematopoietic stem cells."
30 attendees, 1 hour prep/1 hour contact

Invited Speaker: Fenway Community Health Center, "AIDS-related neoplasms."
30 attendees, 1 hour prep/1 hour contact

1996 Hematology/Oncology Research Medical Grand Rounds: Brigham and Women's Hospital/Beth Israel Hospital, "Recent developments in AIDS malignancies."
40 attendees, 1 hour prep/1 hour contact

Dermatology Grand Rounds: Harvard Medical School, "Kaposi's sarcoma."
50 attendees, 1 hour prep/1 hour contact

1997 Oncology Grand Rounds: Salem Hospital, "HIV-related malignancies."
25 attendees, 1 hour prep/1 hour contact

Grand Rounds: St. Vincent's Hospital, "Cytokines in HIV disease."
20 attendees, 1 hour prep/1 hour contact

Grand Rounds: Roswell Park Cancer Institute, "AIDS-related malignancies."
35 attendees, 1 hour prep/1 hour contact

Oncology Rounds: Salem Hospital, "HIV-related malignancies."
20 attendees, 1 hour prep/1 hour contact

Hematology/Oncology Grand Rounds: Columbia-Presbyterian Medical Center,

"AIDS-related malignancies."
35 attendees, 1 hour prep/1 hour contact

Transfusion Medicine Grand Rounds: Brigham & Women's, "Case Discussion; Preliminary results of mononuclear cell collection."
20 attendees, 1 hour prep/1 hour contact

1998 Hematology/Oncology Grand Rounds: St. Elizabeth's Medical Center, "AIDS-related malignancies."
30 attendees, 1 hour prep/1 hour contact

Arthur Ashe Program in AIDS Care, Practice of AIDS Medicine course: Harvard AIDS Institute, Boston, MA. "AIDS Malignancies, Hematologic Complications and Immune Based Therapies."
25 attendees, 2 hours prep/1 hour contact

Transfusion Medicine Grand Rounds: Brigham & Women's Hospital, "Negative regulators of stem cells."
25 attendees, 2 hours prep/1 hour contact

1999 Arthur Ashe Program in AIDS Care, Practice of AIDS Medicine course: Harvard AIDS Institute, Boston, MA. "HIV-related Malignancies and Hematologic Complications."
25 attendees, 2 hours prep/1 hour contact

2000 Hematology/Oncology Grand Rounds: Pennsylvania Hospital, "Malignant complications of AIDS."
40 attendees, 2 hours prep/1 hour contact

Dana-Farber/Partners Cancer Care Grand Rounds: Massachusetts General Hospital, "Making stem cells behave."
30 attendees, 2 hours prep/1 hour contact

Harvard Medical School, Bone Marrow Transplant Grand Rounds: Dana-Farber Cancer Institute, "Designing rational strategies for stem cell manipulation."
50 attendees, 1 hour prep/1 hour contact

Arthur Ashe Program in AIDS Care, The Practice of AIDS Medicine Course: Harvard AIDS Institute, Boston, MA. "HIV-related malignancies and hematologic complications."
25 attendees, 1 hour prep/1 hour contact

Medical Grand Rounds: Massachusetts General Hospital, "Stem Cells: Forever Young?"
60 attendees, 6 hours prep/1 hour contact

Gastrointestinal Research Seminar Series: Massachusetts General Hospital, "Stem Cell Governance."
20 attendees, 2 hours prep/1 hour contact

2001 New England Regional Primate Research Center Seminar Series, New England Regional Primate Research Center, Massachusetts, "Stem cells: designing rational strategies for manipulation."
40 attendees, 2 hours prep/1 hour contact

Invited Speaker: Chief's Conference, Cancer Center Seminars in Hematology and Oncology, Massachusetts General Hospital, Boston, MA. "Control Points in Stem Cell Proliferation and Differentiation."

Immunology Seminar, Massachusetts General Hospital, "Stem cells: designing rational strategies for manipulation."
50 attendees, 1 hour prep/1 hour contact

Medical Grand Rounds, Lowell General Hospital, "Stem cells: what they do, why, how and where are we now?"
50 attendees, 2 hours prep/1 hour contact

Renal Unit Seminar, Massachusetts General Hospital, "Decision points in stem cell regulation." 50 attendees, 3 hours prep/1 hour contact

Medical Services Attending
1 month/year, 4 hours prep/48 hours contact
2 Junior Residents, 1-4 Interns, 1-2 Students

Harvard Medical School, Bone Marrow Transplant Rounds, Dana-Farber Cancer Institute. "Ex vivo strategies to encourage T cell regeneration."
50 attendees, 2 hour prep/1 hour contact

2002 Dana-Farber/Partners CancerCare Grand Rounds: Massachusetts General Hospital, "Altering adult stem cell decision points to direct stem cell therapies"
40 attendees, 2 hours prep/1 hour contact

Medical Grand Rounds: Massachusetts General Hospital, "Immune Regeneration after Cancer or AIDS Therapy." 60 attendees, 6 hours prep/1 hour contact

Harvard Immunology Program: Harvard Medical School, "Microenvironmental effects on Stem Cells." 100 attendees, 3 hours prep/2hour contact

Center for Blood Research Seminar Series, Harvard Medical School: "Microenvironmental effects on primitive hematopoietic cells." 60 attendees, 2

hours prep/1hour contact

2003 Hematology-Oncology Grand Rounds, Beth Israel Deaconess Medical Center, Boston, MA. "Can we make stem cells behave?" 30 attendees, 2 hours prep/1 hour contact time

Invited Speaker: Massachusetts General Hospital, Scientific Advisory Committee Meeting, Boston, MA. "Toward the rational manipulation of stem cells." 100 attendees, 3 hours prep/1 hour contact time

Hematology Division seminar series, Brigham and Women's Hospital. Invited speaker: "What bone does for bone marrow." 30 attendees, 3 hours prep/1 hour contact time

BioMatrix Program, Harvard-MIT Division of Health Sciences and Technology: Stem Cell Research Panel participant. 60 attendees, 1 hour prep/2 hours contact time

Hematology/Oncology Program, Children's Hospital Medical Center, Dana Farber Cancer Institute/Harvard Cancer Center: "Defining and working the stem cell niche." 50 attendees, 3 hours prep/1 hour contact time

Center for Engineering in Medicine, Massachusetts General Hospital: "Microenvironmental Control of Stem Cells". 35 attendees, 2 hours prep/1 hour contact time

Cutaneous Biology Research Center, Massachusetts General Hospital, Boston, MA: ""Identifying and manipulating stem cell niche." 100 attendees, 1 hour prep/5 hours contact time

2004 Rheumatology Grand Rounds Dana Farber Cancer Center, Boston, MA. "Stem Cells" 80 attendees, 2 hours prep/1 ½ hours contact time

Rheumatology Grand Rounds, Massachusetts General Hospital, Boston, MA. "Stem Cells" 30 attendees, 2 hours prep/1 ½ hours contact time

Medical Grand Rounds, West Roxbury VA Medical Center, Boston, MA. "Stem cells: the basics and beyond" 100 attendees, 1 hour prep/1 hour contact

Invited panelist: Alumni/ae Day Symposium "The Ethical Complexities of Embryonic Stem Cell Research", Harvard Divinity School, Cambridge, MA. "Introducing the Harvard Stem Cell Institute."

Biomaterials and Tissue Engineering in Medical Devices and Artificial Organs Course (HST-521), Harvard-MIT Division of Health Sciences and Technology

Invited Speaker: "Cells for Tissue Engineering"
12 graduate student participants, 1 hour/2 hours contact time

Biomedical Engineering Seminar Series: Innovation in Biomedical Engineering and Biomedical Sciences, Harvard-MIT Division of Health Sciences and Technology
Invited Speaker: "Harnessing the body's endogenous potential for tissue regeneration by stem cells"
50 graduate student participants, 1 hour prep/1 hour contact time

2005 Tools of Human Investigation course, MGH Department of Medicine
Invited lecturer: "Stem Cell Research"
? residents, ? hours prep/1 1/2 hours contact time

d. Continuing Medical Education:

1993 Intensive Review of Oncology, Harvard Medical School
Lecturer: "AIDS-related neoplasms."
350 participants, 3 hours prep/1 hour contact

Intensive Review of Hematology and Hematologic Oncology, Harvard Medical School
Invited Speaker: "HIV infection: hematologic manifestations."
75 participants, 3 hours prep/1 hour contact

1996 AIDS Medicine: An Intensive Course, Harvard Medical School
Invited Speaker: "AIDS malignancies."
350 participants, 3 hours prep/1 hour contact

Infectious Diseases of Adults Postgraduate Course, Massachusetts General Hospital
Invited Speaker: "AIDS-associated malignancies."
350 participants, 2 hours prep/1 hour contact

1998 AIDS Medicine: An Intensive Course, Harvard Medical School
Invited Speaker: "AIDS malignancies."
350 participants, 3 hours prep/1 hour contact

AIDS-associated Malignancies: Biology and Clinical Management, University of California, San Francisco
Invited Speaker: "Hematologic complications of and approaches to HIV Disease."
2 hours prep/1 hour contact

1999 Pharmacy Continuing Education Program, Massachusetts College of Pharmacy and Health Sciences

Invited Speaker: "Erythropoietin in cancer and AIDS."
12 participants, 2 hours prep/1 hour contact

HIV, Cancer and Skin Disorders Conference, New England AIDS Education and Training Center
Invited Speaker: "HIV-related cancers."
35 participants, 2 hours prep/1 hour contact

Cancer Medicine and Hematology Postgraduate Course, Harvard Medical School
Invited Speaker: "Hematologic and neoplastic aspects of HIV infection."
450 participants, 2 hours prep/1 hour contact

AIDS Medicine: An Intensive Course, Harvard Medical School
Invited Speaker: "AIDS Oncology."
75 participants, 1 hour prep/1 hour contact

2000 AIDS-associated Malignancies: Biology and Clinical Management, University of California, San Francisco
Invited Speaker: "Adoptive cell transfer in the treatment of HIV and HIV-lymphoma."
2 hours prep/1 hour contact

Cancer Medicine and Hematology Postgraduate Course, Harvard Medical School
Invited Speaker: "Hematologic and neoplastic aspects of HIV infection."
350 participants, 2 hours prep/1 hour contact

AIDS Medicine: An Intensive Course, Harvard Medical School
Invited Speaker: "AIDS Oncology."
75 participants, 1 hour prep/1 hour contact

2001 Cancer Medicine and Hematology Postgraduate Course, Harvard Medical School
Invited Speaker: "Hematologic and neoplastic aspects of HIV infection."
350 participants, 2 hours prep/1 hour contact

AIDS Medicine: An Intensive Course, Harvard Medical School
Invited Speaker: "AIDS Oncology."
75 participants, 1 hour prep/1 hour contact

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|---|---|
| 2002 | Cancer Medicine and Hematology Postgraduate Course, Harvard Medical School<br>Invited Speaker: "Hematologic and neoplastic aspects of HIV infection."<br>350 participants, 3 hours prep/1hour contact |
| 2003 | Current Progress in Tissue Engineering Review Course, Harvard Medical School<br>Invited Speaker: "Stem cell interactions with their microenvironment or what bone does for bone marrow." 100 participants, 3 hours prep/1 hour contact time |
| | Cancer Medicine and Hematology Postgraduate Course, Harvard Medical School<br>Invited Speaker: "Hematologic and Neoplastic Aspects of HIV Infection."<br>150 participants, 4 hours prep/1 hour contact time |
| 2004 | |
| | Cancer Medicine and Hematology Postgraduate Course, Harvard Medical School<br>Afternoon Session Chair. 150 participants, 4 hours prep/1 hour contact time |

e. Advisory and Supervisory Responsibilities

| | |
|---|---|
| 1983 | Harvard College Advisor: Co-chair, Dudley House Committee: Member, 5-10 students/year, 2 hour contact/3 hour prep time each/Advising |
| 1986-present | Harvard College Dudley House Committee: Member, 1-2 students/year |
| 1990-1992 | Harvard University AIDS Institute 1 post-doctoral fellow per year/150 hours/year: Supervisor/Mentor |
| 1991 | Harvard University AIDS Institute post-doctoral fellow: 100 hours/year: Advisor/Mentor |
| 1990-present | Post-doctoral research fellow: Supervisor, 1-10 scientists/year, 100 hours/year |
| 2000-present | Harvard University, Division of Medical Sciences: graduate student supervisor, 1 student/year/100 hours/year |
| 2002-present | Oxford University, U.K.: graduate student co-supervisor, 1 student/year/100 hours/year |
| 2003-present | Harvard College, Molecular and Cellular Biology: undergraduate student supervisor, 1 student/year/50 hours/year |
| 2003-present | Harvard Medical School Scholars in Clinical Science Program mentor: postdoctoral student advisor, 1 student/year/? hours per year |

2003-present Harvard-MIT Division of Health Sciences and Technology HST 160 Clinical Mentor Program: clinical mentor for medical student, 1 student/year/10 hours per year

2004-present Harvard-MIT Division of Health Sciences and Technology: graduate student supervisor, 1 student/year/20 hours per year

2004-present Bucknell University Externship Program: undergraduate student mentor, 1 student/year/2 days per year

f. Advisees and Trainees

| Duration of Training | Name | Current Position |
|---|---|---|
| 1999-Present | Adams, Gregor, Ph.D | Postdoctoral Fellow, Massachusetts General Hospital |
| 2001-Present | Attar, Eyal, M.D. | Postdoctoral Fellow, Massachusetts General Hospital |
| 2000-Present | Cohen, Kenneth, M.D. | Postdoctoral Fellow, Massachusetts General Hospital |
| 2003-Present | Heather Fleming, Ph.D. | Postdoctoral Fellow, Massachusetts General Hospital |
| 2003-Present | Haspel, Richard, M.D., Ph.D. | Postdoctoral Fellow, Massachusetts General Hospital |
| 2003-Present | Janzen, Viktor, M.D. | Postdoctoral Fellow, Massachusetts General Hospital |
| 2004-Present | Mukherjee, Siddhartha, M.D., Ph.D. | Postdoctoral Fellow, Massachusetts General Hospital |
| 2002-Present | Orford, Keith, M.D., Ph.D. | Postdoctoral Fellow, Massachusetts General Hospital |
| 2001-Present | Suscovich, Todd | Graduate student, Harvard University |
| 1999-Present | Saito, Yoriko, M.D. | Postdoctoral Fellow, Massachusetts General Hospital |
| 2003-2004 | Sipkins, Dorothy, M.D., Ph.D. | Postdoctoral Fellow, Massachusetts General Hospital |
| 1998-Present | Wang, Zhengyu, Ph.D. | Postdoctoral Fellow, Massachusetts General Hospital |
| 2002-Present | Zhang, JieLin, M.D. | Visting scientist, BethIsrael Deaconess Hospital |
| 1992-1994 | Berardi, Anna, Ph.D. | Research Scientist, Institute Gustave Roussy |
| 1997-2000 | Brander, Christian, Ph.D. | Assistant Professor, Harvard Medical School |
| 1995-2001 | Carlesso, Nadia, Ph.D., M.D. | Assistant Professor, Harvard Medical School |
| 1994-2000 | Cheng, Tao, M.D. | Director, Stem Cell Biology, |

| | | |
|---|---|---|
| | | Asst. Professor, U of Pittsburgh |
| 1993-1995 | Columbyova, Lucia, M.D. | Clinical practice |
| 1996-1997 | Daga, Antonio, M.D., Ph.D. | Assistant in Medicine, University of Genoa, Italy |
| 1998-2000 | Evans, Richard, M.D. | Lecturer, University of Wales |
| 1992-1994 | Feder, David, M.D. | Res Fellow, McGill Univ. (now deceased) |
| 2001-2004 | Forkert, Randolf, M.D. | 4th year resident, Medizinische Universitaetspoliklinik Bonn, Germany |
| 1993-1995 | Franken, Michael, M.D. | Section Director, Genzyme Corporation |
| 2001-2003 | Gallazi, Anna, M.D. | Research Fellow, Mass. General Hospital |
| 1996-1998 | Gardner, Jason, Ph.D. | Sr. Scientist, Chiron Pharmaceuticals |
| 1996-1997 | Ishiyama, Taijiro, M.D. | Asst. Prof., Showa Univ. Sch. Of Med., Japan |
| 2003-2004 | Lin, Chou-Wen, Ph.D. | |
| 1998-2000 | Miura, Nobuyuki, M.D., Ph.D. | Asst. Prof., Pediatrics, Saitama Medical School, Japan |
| 1999-2000 | O'Connor, Paula, M.D. | Program Leader, Genentech |
| 2001-2003 | Patel, Dipti, M.D. | Northern Virginia Oncology Associates |
| 2001-2004 | Robertson, Paul, M.R.C.P. | Senior SHO in Infectious Diseases, Gartnavel Hospital, Edinburgh |
| 2001-2003 | Rodrigues, Neil | Graduate student, Oxford University, UK |
| 1999-2000 | Sarmento, Leonor, B.S. | Graduate Student, University of Lisboa, Portugal |
| 1994-1999 | Shen, Hongmei, Ph.D. | Assistant Professor, University of Pittsburgh |
| 1999-2001 | Stier, Sebastian, M.D. | Clinical trainee, University of Bonn, Germany |
| 2000-2002 | Szczepiorkowski, Zbigniew, M.D., Ph.D. | Assistant Professor, Dartmouth Medical School |
| 1998-2000 | Whelan, John Patrick, M.D., Ph.D. | Instructor, Harvard Medical School |
| 1989-1990 | Woon, Annie, M.D. | Instructor, Harvard Medical School |

2. Regional, National or International Contributions

   a. Invited presentations

1989 Invited speaker: American Red Cross XXth Annual Scientific Symposium. Hematopoietic Growth Factors in Transfusion Medicine. "GM-CSF in AIDS."

Invited speaker: Immunotoxicology Discussion Group Spring Conference on Safety Assessment of Cytokines. "GM-CSF in AIDS."

Invited speaker: American College of Physicians - University of Connecticut Symposium. "What's New in Internal Medicine. Hematopoietic Growth Factors."

1990 Invited speaker: 15th International Cancer Congress. Satellite Symposium on Cytokines in Tumor Therapy. "GM-CSF/Interferon/AZT for AIDS-associated Kaposi's Sarcoma."

Invited speaker: American Cancer Society. 22nd Annual Medical Symposium. "AIDS related Neoplasms."

Invited speaker: Medical College of Virginia Hematopoietic Growth Factor Symposium. "Applications of Growth Factors in the Treatment of AIDS."

1991 Invited plenary session speaker: International Society for Experimental Hematology. Parma, Italy. "Hematopoietic Abnormalities Associated with AIDS."

Invited speaker: New York Medical College Symposium on Cytokines. "Growth Factors in AIDS."

Invited speaker: Annual Meeting, New England Cancer Society. "AIDS Lymphoma and Kaposi's Sarcoma."

Invited speaker: Community Research Initiative of New England. "Colony Stimulating Factors: G-CSF, EPO, and Others in AIDS."

Invited speaker: Seventh Annual Review of Infectious Diseases for the Specialist. Rose Medical Center, Denver, CO. "Cytokines in AIDS."

1992 Invited speaker: International Conference on Growth Factors in Cancer Therapy. Nashville, TN. "Cytokines in AIDS."

Invited speaker: American Cancer Society, Brigham and Women's Hospital: William C. Maloney Symposium on Advances in Clinical Hematology. "Hematologic Aspects of HIV disease."

Invited speaker: Advances in Transfusion Medicine and Immunohematology Course: Yale University and Harvard University. "Biologic Therapies in

AIDS."

Invited speaker: Hartford Hospital AIDS Program Symposium. "AIDS-related Malignancies."

1993 Invited speaker: 3rd International Symposium on Cytokines in Hematology, Oncology and Immunology Satellite Symposium. Hannover, Germany. "Growth Factors in AIDS."

Invited speaker: Academy of Clinical Laboratory Physicians and Scientists. 28th Annual meeting. New Haven, CT. "Hematopoietic Abnormalities in AIDS."

Invited speaker: Tufts University. Symposium on Clinical Applications of Biologic Agents and Growth Factors in Cancer Therapy. "Cytokines in AIDS."

Invited speaker: Henry Ford Hospital. Hematology Malignancy Symposium. "AIDS-associated Malignancies."

1994 Invited speaker: Memorial Sloane-Kettering Cancer Center, New York, NY. "Isolation and Characterization of Quiescent, Multipotent Hematopoietic Progenitor Cells."

Invited speaker: 5th Bicon: Biennial Conference on Chemotherapy of Infectious Diseases and Malignancies, Salzburg, Austria. "Hematopoietic Growth Factors in the Treatment of HIV-infections."

Invited speaker: University of Indiana, Wells Center for Pediatric Research. Indianapolis, IN. "Isolation and Characterization of Quiescent, Multipotent Hematopoietic Progenitor Cells."

Invited speaker: Harvard Medical School New England Dermatological Society. Boston, MA. "Liposomal Daunorubicin for Kaposi's Sarcoma."

Invited Speaker: 2nd International Conference on Growth Factors in Hematology and Oncology. Atlanta, GA. "Growth Factors in AIDS."

Invited Speaker: Immunex Regional Meetings, Indianapolis, IN. "Cytokines in the Management of HIV Disease."

Invited Speaker: University of Sourthen California School of Medicine. Los Angeles, CA. "Effect of HIV on Bone Marrow Function".

Invited Speaker: The Institute for Medical Studies; Teleconference. "Cytokines in the Treatment of AIDS."

1995 Invited Speaker: New York University Medical Center, New York, NY "Functional Isolation and Characterization of Stem Cells."

Invited Speaker: 3rd International Conference Clinical Application of Cytokines and Growth Factors in Hematology/Oncology. Atlanta, GA. "Use of Growth Factors for AIDS."

Invited Speaker: 4th International Symposium on Immunotoxins. "Combined Immunotoxin and Chemotherapy for initial treatment of AIDS lymphoma." Hollings Cancer Center, South Carolina.

Invited Speaker: Chiron Corporation, San Francisco, CA. "Functional Isolation and Characterization of Stem Cells."

Invited Speaker: University of Pennsylvania Medical Center, Institute for Human Gene Therapy.

Invited Speaker: Walter Reed Army Institute of Research, Division of Retrovirology. Rockville, MD. "Functional Isolation and Characterization of Human Hematopoietic Stem Cells."

Invited Speaker: Fanconi Anemia Annual Scientific Symposium. Boston, MA. "Novel methods of Isolating Stem Cells."

Roundtable Symposium Invited Speaker: 2nd National Conference. Human Retroviruses and Related Infections. The American Society for Microbiology. Washington, DC. "Immune Reconstitution."

Invited Speaker: Project Inform. Immune Restoration Think Tank: The Dobson Project. Houston, Texas.

Invited Speaker: LAPAF and Immunex Corporation. Los Angeles, CA. "Developing HIV therapies from a Hematologist's view."

Invited Speaker: AIDS Provider Group. Los Angeles, CA. "Cytokines in HIV disease."

1996 Chair: International Symposium on Immunodeficiency and its relation to lymphoid and other malignancies. Berlin, Germany. "HIV- associated malignant lymphomas."

Invited Speaker: University of Massachusetts Medical Center, Worcester, MA. "Mapping Gene Expression During Differentiation of Individual Hematopoietic Cells."

Invited Speaker: Boston University School of Medicine, Whitaker

Cardiovascular Institute, Boston, MA. "Modeling lineage commitment in human hematopoietic cells."

Invited Speaker: The Third Conference on Retroviruses and Opportunistic Infections. Dallas, TX. ProMedica

Invited Speaker: Lindsley F. Kimball Research Institute, New York Blood Center, New York, NY. "Modeling lineage commitment in human hematopoietic cells."

Invited Speaker: International Workshop, Gene Targeting in Hematology/Oncology. Genova, Italy. "Modeling stem cell gene therapy for AIDS.

Invited Speaker: Sylvester Comprehensive Cancer Center, University of Miami, Florida. "AIDS-related malignancies."

Invited Speaker: Boston Users Group for Cytometry, "Function-based stem cell isolation."

Invited Speaker: Wayne State University/Harper Hospital, Detroit, MI. "Treatment of Kaposi's Sarcoma: Future Directions."

Invited Speaker: Martin Memorial Medical Center, Stuart, FL. "AIDS-related malignancies."

1997 Invited Speaker: The Center for Blood Research, Boston, MA. "Characterization of human hematopoietic stem cells."

Roundtable discussion: Sequus Pharmaceuticals, Inc. New York, NY. "Case Studies in Kaposi's Sarcoma: A Multidisciplinary Approach to Treatment."

Program Convener: 4th Conference on Retroviruses and Opportunistic Infections. Washington, DC. "Non-KS Malignancies: Bench to Bedside."

Invited Speaker: Current Issues and Future Directions in the Prevention of Invasive Fungal Infections. Los Angeles, CA. "Who is to benefit from cytokine therapy: Targeting patients at risk."

Invited Speaker: University of Alabama AIDS Research Center. Birmingham, AL. "AIDS-related lymphoma."

Invited Speaker: South Florida Oncology Review. Baco Raton, Fl. "AIDS-related malignancies."

Invited Speaker: Massachusetts General Hospital, Boston, MA. Gastrointestinal

Unit Research Seminar. "Human hematopoietic stem cells."

Invited Speaker: Amgen, SCF/AIDS Preclinical Meeting, Westlake Village, CA. "SCF and the anemia, hematology, and immunology of AIDS."

Invited Speaker: Amgen, New Seabury, MA. "The clinical management of AIDS: antivirals, protease inhibitors and G-CSF Use."

Invited Speaker: 2nd Joint Conference NIAID SPIRAT/NCDDG-HIV programs, Vienna, VA. "New Opportunities for HIV therapy: From discovery to Clinical Proof-of-Concept."

1998 Invited Speaker: Indiana University, Indianapolis, IN. "Chemokine receptor function in hematopoietic stem cells."

Invited Speaker: Ortho Biotech, The Distinguished Faculty Program at Correctional Medical Service, Dedham MA "Hematologic aspects of HIV disease."

Invited Speaker: Massachusetts General Hospital, Boston, MA. Infectious Diseases of Adults Postgraduate Course. "AIDS-associated malignancies."

Invited Speaker: Ortho Biotech, The Distinguished Faculty Program. Shattuck Hospital, Boston, MA. "Hematologic aspects of HIV disease."

Invited Speaker: NIH/NHLBI, Bethesda, MD. "Negative regulators of hematopoietic stem cells."

Invited Speaker: Ortho Biotech, The Distinguished Faculty Program. Fenway Community Health Center, Boston, MA. "Hematologic aspects of HIV disease."

1999 Invited Speaker: Harvard AIDS Institute, International Symposium on HIV, Leukemia and Opportunistic Cancers, Marrakech, Morocco. "The Hematopoietic Stem as Target and Tool in HIV Disease."

Invited Speaker: Advanced Biotechnology Center, International Workshop, Verona, Italy. "Updates in Immunohematology and Oncology: From Cell Progenitors to Effector Functions."

2000 Invited Speaker: BIO 2000, 4th Annual Tech Transfer Forum, Boston, MA. "Novel Strategies for Modulating Immune Cell Localization".

Invited Speaker: Division of Hematology/Oncology Conference, University of Pennsylvania, Center for AIDS Research. "Defining Molecular Targets for Stem Cell Manipulation."

Roundtable Discussion Chair: 4th International AIDS Malignancy Conference, National Institutes of Health, Bethesda, MD. "New Directions in AIDS Lymphoma Treatment."

Invited Speaker: Hematology/Oncology Teaching and Research Seminar, New York University Medical Center. "Making Stem Cells Behave."

Invited Speaker: Institute of Human Virology Seminar, Virology Institute, Baltimore, MD. "Molecular targets for stem cell engineering."

Invited Speaker: Holland Laboratory Hematopoiesis Department Seminar, American Red Cross, Rockville, MD. "Molecular brakes on Stem Cell Proliferation."

Invited Speaker: 12th Annual International Fanconi Anemia Scientific Symposium, Amsterdam, The Netherlands. "The boundary between stem and progenitor cells is marked by distinct molecular regulators of cell cycle entry."

2001 Invited Speaker: UMASS Medical Center, Worcester, MA. "Stem cells: designing rational strategies for manipulation."

Invited Speaker: Ortho Biotech and Institute for Continuing Education Program, Living Longer, Living Stronger: Maintaining the Quality of Life for Patients with Anemia and HIV Infection. Fenway Community Health Center, Boston, MA "Hematological aspects of HIV Disease."

Indiana University School of Medicine Combined Seminar Series, Indiana University, Indiana, "Stem cells: designing rational strategies for manipulation."

Invited Speaker: Biology Department Seminar, Bucknell University, Lewisburg, PA. "Stem cell research."

Invited Speaker: HIV/AIDS Symposium, Immune Control of Paediatric and Adult HIV Infection in South Africa, Durban, South Africa. "AIDS-related malignancies."

Invited Speaker: Special Seminar, Genzyme Corporation, Framingham, MA. "Stem cells: designing rational strategies for manipulation."

Invited Speaker: Hematology Seminar Series, Department of Hematology, Yale University School of Medicine, New Haven, CT. "Designing rational strategies for stem cell manipulation."

Invited Speaker: Department of Cell Biology Seminar, Georgetown

University, Washington, DC. "Stem cells: designing rational strategies for manipulation."

Invited Speaker: National Center for AIDS Prevention and Control, Beijing, People's Republic of China. "Advances in understanding stem cells and their clinical implications."

Invited Speaker: Chinese Academy of Sciences, Beijing, People's Republic of China. "Strategies for achieving stem cell based therapies for AIDS."

Invited Speaker: Changhai Hospital, Shanghai Second Military Medical University, Shanghai, China. "Strategies for achieving stem cell based therapies for AIDS."

Invited Speaker: National Cancer Institute, Center for Cancer Research Grand Rounds, National Institutes of Health, Bethesda, MD. "Altering Adult stem cell decision points to direct stem cell therapies."

Invited Speaker: Department of Biomedical Research Division of Hematology and Oncology, Hematology/Oncology Grand Rounds, St. Elizabeth's Medical Center, Boston, MA. "Making stem cells behave."

2002 Invited Speaker: Hematology and Medical Oncology Grand Rounds, Memorial Sloan-Kettering Cancer Center, New York, NY. "Toward the rational manipulation of hematopoietic stem cells."

Invited Speaker: Division of Hematology-Oncology Seminar Series, Tufts University School of Medicine, New England Medical Center, Boston, MA. "Toward the rational manipulation of hematopoietic stem cells."

Invited Speaker: Department of Microbiology and Immunology Seminar Series, University of Montreal, Montreal, Canada. "Toward the rational manipulation of hematopoietic stem cells."

Invited Speaker: Dana-Farber/Partners Cancer Care Grand Rounds, Boston, MA. "Altering Adult Stem Cells Decision Points to Direct Stem Cell Therapies"

Invited Speaker: National Cancer Institute, Mouse Models of Human Cancers Consortium, Somatic and Embryonic Stem Cell Research Symposium, Bethesda, MD. "Molecular mediators of hematopoietic stem cell decision points."

Invited Speaker: The Children's Hospital of Philadelphia, Philadelphia, PA. "Toward the rational manipulation of hematopoietic stem cells."

Invited Speaker: MIT Lincoln Laboratory, New England Bioterrorism

Preparedness Workshop, Lincoln, MA. "Targeting Immunity to Biothreats Through Cell Manipulation."

Invited Speaker: Educational Meeting of the Physicians' Research Network, New York, NY. "Lymphoma in the Setting of HIV."

Invited Speaker: Basic Science Correlates Grand Rounds, Massachusetts General Hospital, Boston, MA. "Rebuilding Immunity after AIDS or Cancer Therapy."

Invited Speaker: Coriel Institute, University of Medicine and Dentistry of New Jersey, Camden, NJ. "Mechanisms governing hematopoietic stem cell localization."

Invited Speaker: Roger Williams Medical Center, Brown University, Providence, RI. "Altering Adult Stem Cell Decision Points to Direct Stem Cell Therapies."

Invited Speaker: American Society of Clinical Oncology Annual Meeting/Educational Symposia, Orlando, FL. "HIV-Related Cancers"

Invited Speaker: Institute of Human Virology, University of Maryland, "Stem cell regulatory mechanisms to guide gene therapy for AIDS."

Invited Speaker: Institute of Hematology, Chinese Academy of Medical Sciences, Tianjing, China. "Perspectives on Stem Cell Research"

Invited Speaker: Hematology/Oncology Research Seminar Series, University of Pennsylvania School of Medicine, Philadelphia, PA. "Location is everything: what the microenvironment does for stem cells."

Invited Speaker: Yale University School of Medicine, New Haven, CT "Toward the rational manipulation of stem cells."

Chair of panel: Dana-Farber Clinical Center Lymphoma and Viral Oncology Programs Minisymposium, Boston, MA. "Viral Pathogenesis of Lymphoma Malignancies."

Invited Speaker: International Meeting of the Institute of Human Virology, Baltimore, MD. "Developing Adult Stem Cell-Based Therapies"
Invited Speaker: Lund University, Lund, Sweden. "Influencing stem cell behavior: Cues from the microenvironment."

2003 Invited Speaker: Medicine Research Seminar Series, The University of Texas, San Antonio, TX. "Stem Cell Function and the Microenvironment Niche"

Invited Panel Speaker: Bioethical Issues Raised By the Mapping of the Human Genome Seminar, Academic Medical Development Company Meeting, Albany, NY. " Stem Cell Research: How Far Should We Go?"

Invited Speaker: Midwest Blood Club Symposium, Cincinnati, OH. "Toward the rational manipulation of stem cells."

Invited Speaker: CIMIT Center for Innovative Technology for Medicine, Boston, MA. "Making stem cells behave."

Invited Speaker: Biology Department Seminar, Bucknell University, Lewisburg, PA. "Stem cells: from biology to clinical use".

Invited Speaker: CIMIT Center for Innovative Technology for Medicine, Boston, MA. "Microenvironment Governing of Stem Cells".

Invited Speaker: American Association of Blood Banks Annual Meeting "Adult Stem Cells and their applications in regenerative medicine".

Invited Speaker: MD Anderson Cancer Center Blood and Marrow Transplantation Research Conference, Houston, TX. "Defining and manipulating the stem cell niche"

Invited Speaker: Dana-Farber/Partners Cancer Care Grand Rounds, Boston, MA. "Prospects for stem cell based therapies."

2004 Invited speaker: New York University, New York, NY. "Defining and manipulating the hematopoietic stem cell niche."

Invited speaker: University of Michigan, Department of Developmental Biology, "Defining and manipulating the hematopoietic stem cell niche."

Invited speaker: Institute of Hematology, Chinese Academy of Medical Sciences, International symposium on stem cells-Scientific, Medical, Societal, and Ethical aspects, Tianjing, China. "Defining and manipulating the stem cell niche".

Invited speaker: Asan-Harvard International Symposium IV, Seoul, Korea. "Defining and manipulating the stem cell niche" and "Mimicking in vivo microenvironments to manipulate stem cells ex vivo."

Plenary speaker: International Society for Stem Cell Research, Boston, MA. "Deconstructing the hematopoietic microenvironment."

Plenary speaker: International Society of Experimental Hematology, New Orleans, LA. "Defining and manipulating the hematopoietic stem cell niche." Also chair of concurrent session "Myeloproliferative Syndromes"

Keynote speaker: Kansas University Medical Center/Stowers Institute for Medical Research First Annual Kansas and Missouri Stem Cell Science Symposium, Kansas City, Missouri. "Normal and Leukemia Stem Cells and their Microenvironment"

Invited speaker: The VII International Meeting on In Utero Stem Cell Transplantation: New Frontiers in Regenerative Therapy, Rome, Italy. "Defining and manipulating the stem cell niche." Also chairman of session "Cord blood and adult stem cells"

Invited speaker: National Cancer Institute/Memorial Sloan-Kettering Cancer Center, 3rd Mouse Models of Hematopoietic Malignancies Workshop, New York, New York. "Defining and manipulating the stem cell niche."

Keynote speaker: Fourth Annual Meeting on Mesenchymal & Non-Hematopoietic Stem Cells: Focus on Adult Stem Cells, New Orleans, LA.

Invited speaker: The University of Texas/Southwestern Medical School, Dallas, TX. "Defining and manipulating the stem cell niche."

Keynote speaker: The American Society of Nephrology Renal Week, St. Louis, MO. "Regenerating Tissues and Organs: Fact or Fantasy?"

Invited speaker: The Leukemia & Lymphoma Society Stohlman Scholar Symposium, Denver, Colorado. "Therapeutic manipulation of the stem cell niche."

Plenary speaker: International Congress of the Cell Transplant Society, Boston, MA. "Hematopoietic stem cells and microenvironment."

Plenary speaker: 2nd Annual Australian National Stem Cell Centre National Conference, Sydney, Australia. "Defining and manipulating the hematopoietic stem cell niche."

Invited speaker: First International Stem Cell Symposium, Weizmann Institute of Science, Rehovot, Israel. "Therapeutic manipulation of the stem cell niche."

b. Professional Leadership Roles Related to Teaching

1991 Educational Session on AIDS: American Society of Hematology Annual Meeting. "Hematologic dysfunction induced by HIV-1."

1993 Educational Session on AIDS, Chair, American Society of Hematology Annual

Meeting.

1994 Program Committee and Chairperson of Session: 30th Annual Meeting of the American Society of Clinical Oncology. "Novel Approaches to AIDS-related Cancers/Protection and Stimulation of Normal Tissues."

Simultaneous Session Co-Chairman, American Society of Hematology Annual Meeting. "Retroviral Diseases."

1995 Simultaneous Session Moderator, American Society of Hematology Annual Meeting. "Retroviral Diseases."

1996-1997 Program Committee: 1st International AIDS Malignancy Conference.

1997 Session Organizer and Chair: 4th National Conference on Human Retroviruses and Related Infections. American Society of Microbiology.

Session Chairperson: 1st International AIDS Malignancy Conference.

1997-1998 Program Committee and Section Chair: 34th Annual Meeting of the American Society of Clinical Oncology.

1998 Program Committee and Section Chair: 40th American Society of Hematology Annual Meeting.

Program Committee: 2nd International AIDS Malignancy Conference.

Session Chairperson: 2nd International AIDS Malignancy Conference.

2nd International AIDS Malignancy Conference.

1999 Program Committee and Section Chair: 41st American Society Hematology Annual Meeting.

Program Committee and Section Chair: 35th Annual Meeting of the American Society of Clinical Oncology.

Program Committee: 3rd International AIDS Malignancy Conference.

Session Moderator: Plenary Lecture, 3rd International AIDS Malignancy Conference.

Program Committee: American Society of Microbiology Herpesvirus Meeting.

2000 Program Committee: 4th International AIDS Malignancy Conference.

Oral Session Moderator and Abstract Reviewer: "Immunodeficiency, Including HIV Infection." 42nd Annual Meeting of The American Society of Hematology, San Francisco, CA.

2001 Program Committee: 5th International AIDS Malignancy Conference

Roundtable Discussion Chair: 5th International AIDS Malignancy Conference, National Institutes of Health, Bethesda, MD. "Clinical Issues and New Directions in the Treatment of AIDS Malignancies."

Coordinating Scientific Reviewer: Immunodeficiency and HIV infection, 43rd Annual Meeting of the American Society of Hematology.

L'Association Francaise Contre Les Myopathies (AFM)/Harvard Medical School Steering Committee, Children's Hospital, Boston, MA. "Progress Towards Clinical Gene Therapy."

Invited Speaker, Education Program Session, *HIV*, 43rd Annual Meeting of The American Society of Hematology. "Stem cells in HIV infection."

Invited Speaker, Scientific Program Session, *Thymic Function and Efforts to Enhance Immunologic Recovery After Transplantation,* 43rd Annual Meeting of The American Society of Hematology. " Ex Vivo Differentiation on Three-Dimensional Matrices."

2002 Session Chair, 3rd Stem Cell Gene Therapy Conference, Rockville, MD. "Stem cell gene transfer biology."

Invited Speaker, Education Program Session, HIV-related cancers, 38th Annual Meeting of the American Society of Clinical Oncology. "AIDS-related lymphoma."

Session Chair and Invited Speaker, Institute for Human Virology International Meeting, Baltimore, Maryland. "Stem cell biology."

Abstract review committee, American Society of Hematology annual meeting

2003 Scientific Program Committee, International Society for Experimental Hematology annual meeting

Program Committee and Invited Speaker, 7th International AIDS Malignancy Conference, Bethesda, MD.

2004 Program Committee and Plenary Speaker, International Society for Stem Cell Research Annual Meeting, Boston, MA

Program Committee and Invited Speaker, 8th International AIDS Malignancy Conference, Bethesda, MD

Scientific Program Committee and Plenary Speaker, International Society for Experimental Hematology Annual Meeting, New Orleans, LA

Abstract review committee, American Society of Hematology annual meeting, San Diego, CA

3. Innovative educational programs

1998 Clinical Applications of the Revised European-American Lymphoma Classification (R.E.A.L.). Through highly focused talks and discussion panels, comprised of pathologists and clinicians, this course is used as a teaching tool for clinicians on this new approach to lymphoma classification.

## E. Report of Clinical Activities

1. Hematology/Oncology, Massachusetts General Hospital and Dana-Farber Cancer Institute, 1 Outpatient Clinic/week; daily inpatient care

2. Patient Load
   - 3-15 patients/week
   - high level of care

3. Attending Physician, Hematology consult service, Massachusetts General Hospital (one month annually)

## PART III:Bibliography

### Original Articles


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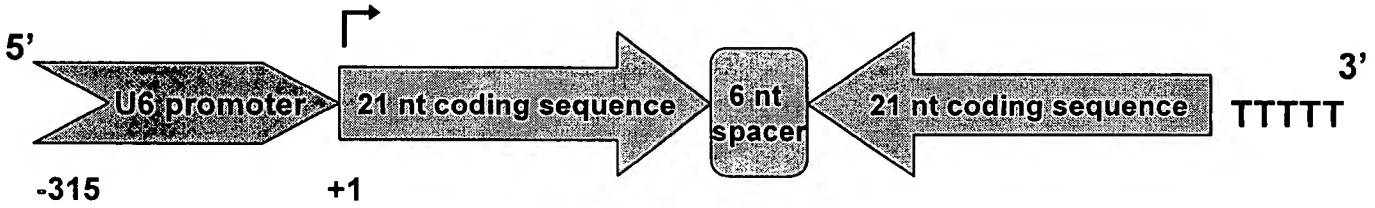
# APPENDIX B

**siRNA**

| | |
|---|---|
| Si-2 | 5' CUU CGA CUU UGU CAC CGA G 3'<br>GAA GCU GAA ACA GUG GCU C |
| Si-2M | 5' CUC GAC UUC GUA CCC GAG 3'<br>GAG CUG AAG CAU GGG CUC |
| HPRT | 5' GUG UCA UUA GUG AAA CUG G 3'<br>CAC AGU AAU CAC UUU GAC C |

**shRNA** Coding sequence

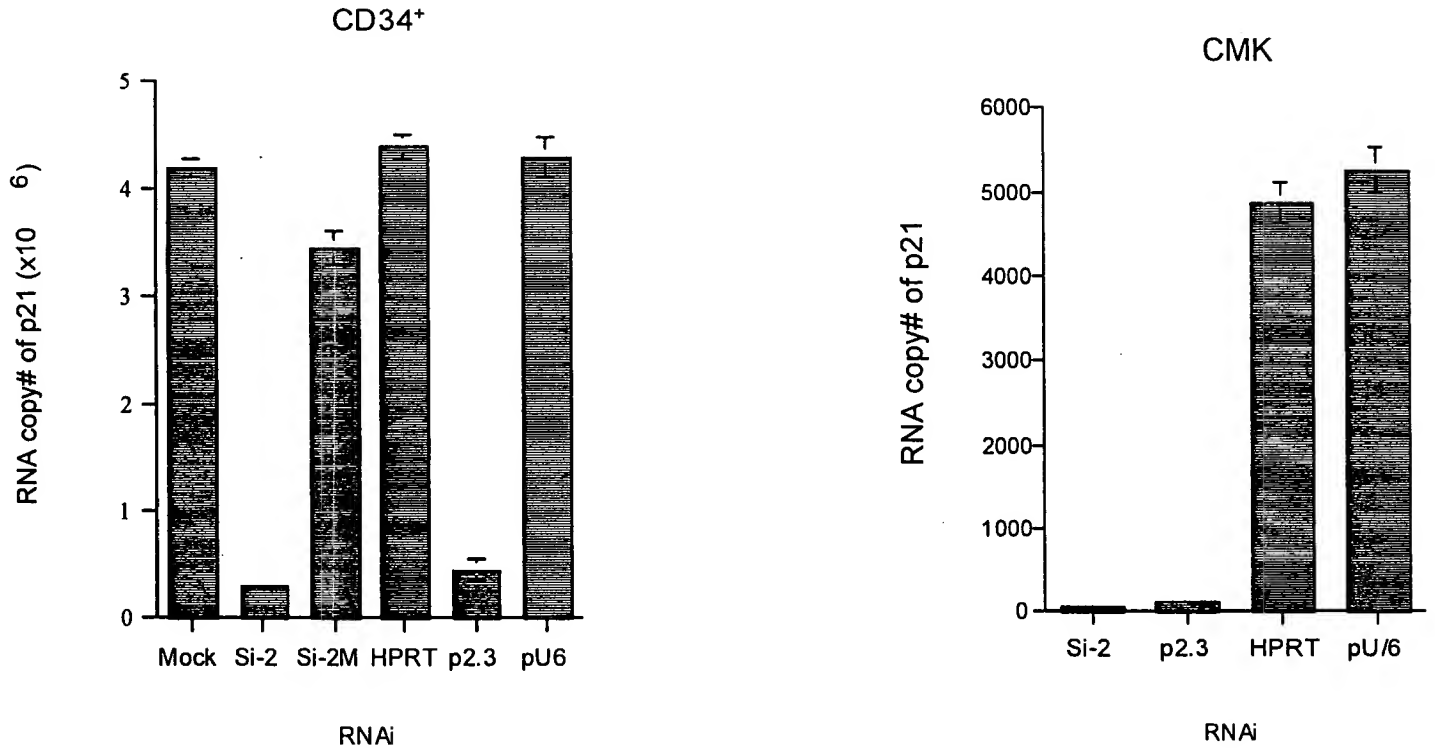
p2.3 5' GGT GAC TTC GCC TGG GAG CGT ATC
GTA ACG CTC CCA GGC GAA GTC ACC 3'

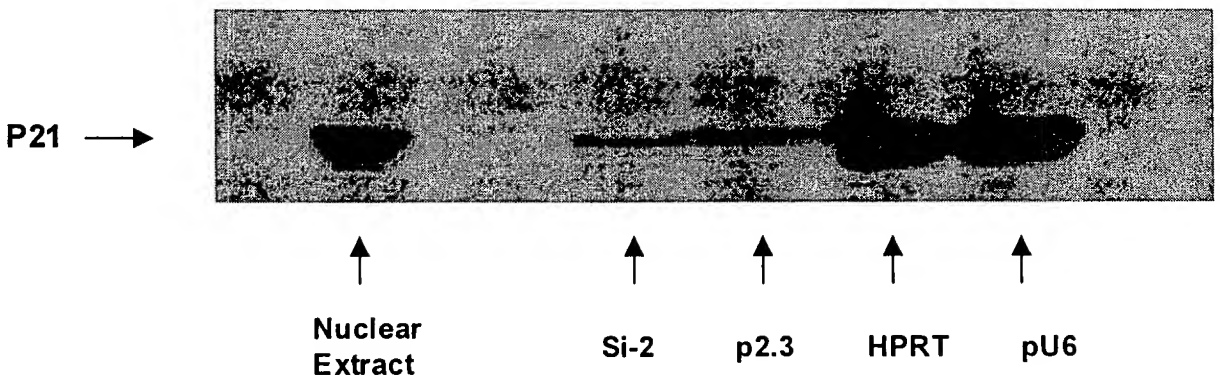



**p21 cDNA**

1 cgtcagaacc catgcggcag caaggcctgc cgccgcctct tggcccagt ggacagcgag
61 cagctgagcc gcgactgtga tgcgctaatg gcgggctgca tccaggaggc ccgtgagcga
121 tggaacttcg actttgtcac cgagacacca ctggagggtg acttcgcctg ggagccgtgtg
Si-2 p2.3
181 cggggccttg gcctgcccaa gctctacctt cccacggggc cccggcgagg ccgggatgag
481 ttccagggtg acagtgagat tcatctcaaa taaatacata aataaaaaac tgtttggtaa
541 tatcttct

# APPENDIX C

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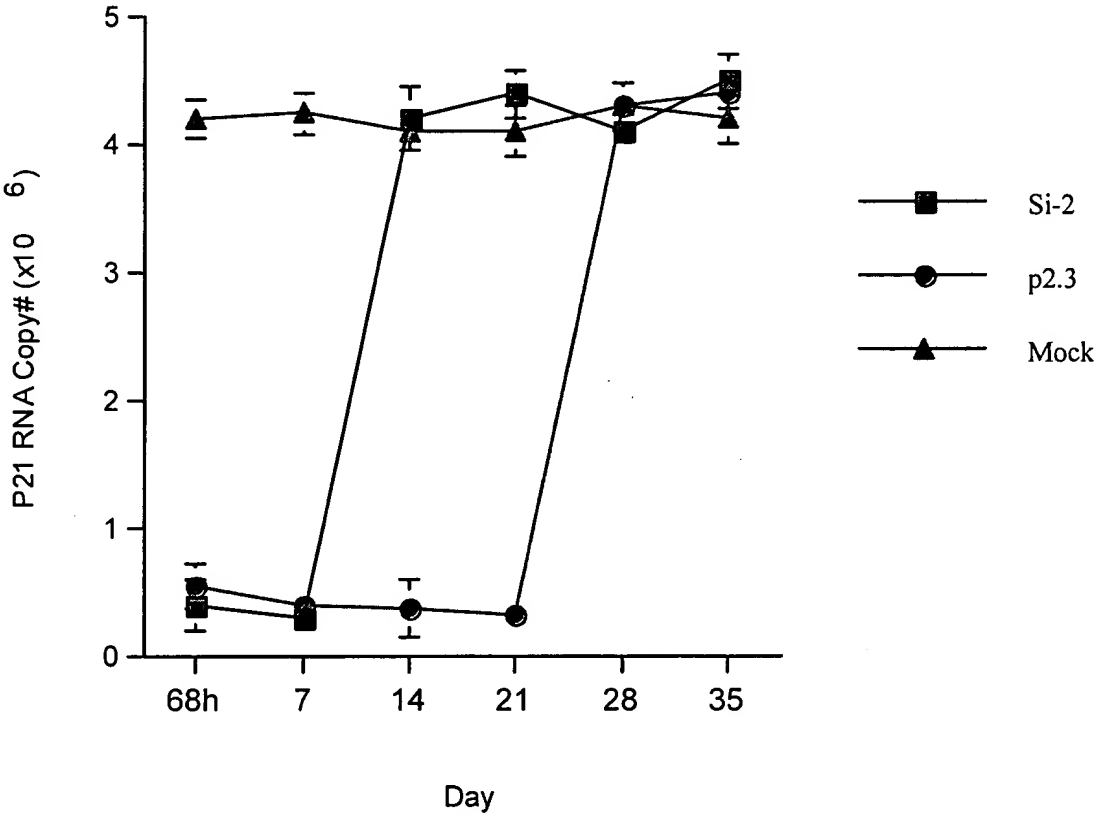
# APPENDIX D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